

REMARKS

This Submission of Request for Continued Examination is in response to the Advisory Action dated July 9, 2004, in connection with the above application.

Applicants submitted a Response and an Amendment on June 15, 2004, including a Declaration under 37 CFR 1.132 by Dr. Parkash Gill. Applicants request entry and consideration of the Response and Amendment, including the Declaration by Dr. Gill. Applicants note that the Amendment was entered for the purpose of appeal and that the Examiner refused to consider the Declaration of Dr. Gill. (See Advisory Action dated July 9, 2004). In addition, Applicants request the Examiner to consider the arguments set forth below.

A. The claims are not obvious in view of Uchida et al. and other references.

Applicants request that the Examiner reconsider a fundamental issue in the prosecution of this application, that being whether the prior art is sufficient to establish a *prima facie* case for obviousness.

Applicants stress that the claims presently pending pertain only to nucleic acids that are modified for use *in vivo* or in cells. According to the Declaration of Dr. Gill, the cited art, Uchida et al., provides dozens of antisense probes that are effective at suppressing VEGF gene expression in a cell-free biochemical assay. However, Dr. Gill notes that none of the antisense probes of Uchida et al. that were tested *in vivo* proved to be effective, either in cell-based assays or in a mouse assay. Thus, according to Dr. Gill, one of ordinary skill in the art, upon reviewing Uchida et al, would not be motivated to modify the probes presented therein for use *in vivo*.

A *prima facie* case of obviousness cannot be made where there is no motivation for one of ordinary skill in the art to modify the cited art so as to arrive at the claimed invention. The Applicants have provided factual evidence, in the form of the expert opinion of Dr. Gill, to demonstrate that one of ordinary skill in the art would not be motivated to modify the probes presented in Uchida et al. for use *in vivo*.

In rebuttal, Examiner writes, "[T]he claims of Uchida et al. are clearly drawn to methods of inhibition of VEGF *in vivo*." Applicants remind that Examiner that the question at issue is not what the Examiner would conclude from a review of the prior art but what one of ordinary skill

in the art would conclude from a review of the prior art, and what modifications to the prior art one of ordinary skill in the art would be motivated to make. The Declaration of Dr. Gill provides evidence of what a practitioner in the field would be motivated to do on the basis of Uchida et al. Per MPEP 2144.08(B), "Office personnel should consider all rebuttal arguments and evidence presented by applicants." MPEP Eighth Edition, Incorporating Revision No. 2, May, 2004. The Examiner has provided no other factual evidence to establish how one of ordinary skill in the art would interpret the teachings of Uchida et al., and accordingly, it is Applicants' position that one of ordinary skill in the art would not find motivation in Uchida et al. to modify the probes disclosed therein for use in vivo.

B. Change of inventorship

Applicants submit herewith a Request for Correction of Inventorship under 37 C.F.R. §1.48(a). This Request is accompanied by a signed statement of the omitted inventor stating that the omission was made without deceptive intent.

C. Conclusion

Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this submission, please charge the fees to our **Deposit Account No. 18-1945**. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit account.

Respectfully Submitted,

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Customer No: 28120
Docketing Specialist
Ropes & Gray LLP
One International Place
Boston, MA 02110
Phone: 617-951-7000



John Quisel, Ph.D.
Reg. No. 47,874